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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,647	04/21/2004	Sharat Singh	033.09-2US	5824

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EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

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08/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/828,647	**Applicant(s)** SINGH ET AL.	
	Examiner Joyce Tung	**Art Unit** 1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 10 July 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *7/23/07*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *21-30*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

The applicant's response filed 7/10/07 to the Office action has been entered. Claims 21-30 are pending.

1. The rejection of claims 21-30 under 35 U.S.C. 112, second paragraph in section 7(a) is withdrawn because of the applicant's argument.

2. The rejection of claims 21-22, 24, and 28 under 35 U.S.C. 102(b) as being anticipated by Grossman et al. (US 5,470,705, issued November 28, 1995) is withdrawn upon reconsideration.

3. Claims 21-30 remain respectively or provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-30 of copending Application No. 10/779255, over claims 1-7 of U.S. Patent No. 6,770439, over claims 1-13 of U.S. Patent No. 7017125 and over claims 1-20 of U.S. Patent No. 6673550 because the terminal disclaimer was not filed.

4. Claims 21-25, and 27-29 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al. (6,027,890) in view of Grossman et al. (US 5,470,705, issued November 28, 1995).

Van Ness et al. disclose a variety of first and second member of a ligand pairs in which one or more members used in the method is tagged (See column 2, lines 14-27) and the tag is cleavable by oxidation (See column 4, lines 16-24). The ligand pair can be an antibody or antibody fragment or nucleic acid molecule/nucleic acid molecule (See column 2, lines 29-44). The tag is detectable by non-fluorescent spectrometry, or potentiometry (See column 2, lines 55 to column 3, lines 1-8) or the tag can be fluorescent labeled and detected by fluorometer (See column 3, lines 37-40). The labile linking group has thioethers, disulfide formation (See column 37, lines 12-26) and sulfoxide (See column 34, lines 39-46). There are more than 500 different

and unique tagged molecules and each tag is unique for a selected nucleic acid fragment or first or second member and may be separately identified (See column 3, lines 29-36). The bound member and unbound member are separated by electrophoresis (See column 3, lines 58-67). The member ligand pair of Van Ness has the same components of the probe set.

However, Van Ness et al. do not disclose the ligand pair having a mobility modifier, which produces a unique electrophoretic mobility.

Grossman et al. disclose that the probe includes a binding polymer, a polymer chain which imparts to that probe, a distinctive ratio of charge/translational frictional drag and a reporter attached to the binding polymer (See column 20, lines 52-57). Grossman et al. also disclose that a ratio of charge/translation frictional drag is distinctive for each different-sequence probe in which addition of charge groups to the polymer chain or the subunit length of the polymer chain can be used to achieve selected ratio of charge/translation frictional drag (See column 11, lines 34-43) and the electrophoretic movement in a non-sieving medium can finely resolved by derivatization with polymer chain having slightly different size and /or charge differences (See column 11, line 46-51).

One of ordinary skill in the art would have been motivated to apply the mobility modifier of Grossman et al., the ratio of charge/translation frictional drag to the ligand pair of Van Ness et al. because as taught by Grossman et al. the ratio of charge/translation frictional drag is distinctive for each different-sequence probe and the electrophoretic movement in a non-sieving medium can finely resolved by derivatization with polymer chain having slightly different size and /or charge differences (See column 11, line 46-51). It would have been prima facie obvious

to have the mobility modifier in the ligand pair of Van Ness et al. to make the claimed probe in the composition.

The response argues that Grossman et al. do not disclose electrophoretic probes that upon cleavage of L produce an eTag reporter comprising a detection group, D, and a mobility modifier, M. Grossman et al. either disclose a set of probes that are not cleaved (column 20, lines 61-column 21, line 15 and Figures 20A-20C), or probes that upon cleavage form two fragments where one of them has the detection group and the other has the mobility modifier (Section D, column 19, line 22 to column 20, line 44 and figures 17A and 17B). Nevertheless, Grossman et al. disclose that in the method the sequence-specific probes are cleaved by 5' to 3' end exonuclease. The released probe is composed of base, reporter and polymer chain, which imparts to the labeled probe, a distinct ratio of charge/translational friction drag (See column 20, lines 19-25). Therefore, the teachings of Grossman et al. satisfy the limitations of the eTag formula. Thus, the rejection is maintained.

5. Claim 26 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al. (6,027,890) in view of Grossman et al. (US 5,470,705, issued November 28, 1995) as applied to claims 21-25, and 27-29.

The teachings of Grossman et al. and Van Ness et al. are set forth in sections 4 above. Grossman et al. do not disclose the molecular weight of the mobility modifier recited as the range of from 30-3000 Daltons.

Grossman et al. disclose a probe composition of detecting a plurality of different sequences in a target sequence involving a plurality of sequence probes (See column 2, lines 54-

64 and column 6, lines 46-54). The number of the probes is six probes, which are added to a target polynucleotide (See column 20, lines 49-51).

Grossman et al. do not explicitly disclose the molecular weight of the mobility modifier. However, the binding polymer and polymer chain contribute to the mobility modifier of probe (See column 3, lines 55-64,). The polymer chain may be polyethylene oxide (PEO) or a polypeptide chain (See column 3, lines 11-18, column 7, lines 39-49). Since these molecules are small molecules, the teachings are inherent that the molecular weight of the mobility modifier would be from 150-5000 Daltons.

One of ordinary skill in the art would have been motivated to apply the molecule weight of binding polymer and polymer chain used in the method of Grossman et al. because Grossman et al. disclose that the binding polymer and polymer chain contribute to the mobility modifier of the probe (See column 3, lines 55-64), the mobility modifier is distinctive for each different-sequence probe (See column 11, lines 34-43) and the electrophoretic movement in a non-sieving medium can finely resolved by derivatization with polymer chain (See column 11, line 46-51). It would have been prima facie obvious to apply the mobility modifier with the molecular weight in the range of from 30-3000 Daltons to make the probe in the composition.

The response argues the same issues as argued above. Thus with the same reasons as set forth in section 4 above, the rejection is maintained.

6. Claim 30 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al. (6,027,890) in view of Grossman et al. (US 5,470,705, issued November 28, 1995) as applied to claims 21-25, and 27-29, further in view of further in view of Breslow et al. (6,331,530, issued Dec 18, 2001).

The teachings of Grossman et al. and Van Ness et al. are set forth in sections 4 above. None of the references addresses the cleavable linkage, which is cleaved by singlet oxygen.

Breslow et al. disclose a linker between two β-cyclodextrin molecules and that a photosensitizer is encapsulated within a matrix, wherein the cleavable linker is cleaved upon exposure to light (See the abstract). Singlet oxygen is produced to cleave the linker (See column 3, lines 47-51).

One of ordinary skill in the art would have been motivated to apply the cleavable linker, which is cleaved upon exposure to light because the active cleaving agent, singlet oxygen is used in the system of Breslow et al. for cancer therapy and this suggests that the active cleaving agent must be very efficient. Thus, it would have been prima facie obvious to apply the cleavable linker, which is cleaved by singlet oxygen as taught by Breslow et al. to make the claimed probe set.

The response argues that Breslow et al. do not disclose that the released molecules are electrophoretically separated and do not disclose electrophoretic probes having a cleavable linkage L. Grossman discloses that the sequence-specific probes are cleaved by 5' to 3' exonuclease (See column 20, lines 19-25). The released probe is composed of base, reporter and polymer chain, which imparts to the labeled probe, a distinct ratio of charge/translational friction drag (See column 20, lines 19-25). Therefore, the teachings of Grossman satisfy the limitations of the eTag fomula. Thus, the rejection is maintained.

Summary

7. No claims are allowable.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung
August 21, 2007

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
8/30/07